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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SHUKLA, RAM R	
ART UNIT	**PAPER NUMBER**
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/057,136	SCHLOM ET AL.	
	Examiner	Art Unit	
	Ram R. Shukla	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-39 and 41-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-39 and 41-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/25/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of the invention of group I, claims 23, 27 and 35 in the reply filed on 5/21/04 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claim 40 has been cancelled.

3. Applicants have amended claims 24-26, 28-34, 36-39 and 41 to depend from claims 23, 27 and 35. New claims 42-59 have been entered. Accordingly, claims 23-39 and 41-59 are pending and under consideration.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 38 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 38 limits the virus of claim 23 to rV-MUC1.

When the claims are analyzed in light of the specification, instant invention encompasses a recombinant pox virus, which comprises a MUC1 fragment that has 10 tandem repeat units. The only description of the virus is provided on page 22 (paragraph 1 and paragraph 2), that relates to the cloning of the MUC1 DNA fragment in a vaccinia virus. In analyzing whether the written description requirement is met for a given invention, it is first determined whether the invention has been described by its complete structure. In the instant case, the only description is the name of the virus (rV-MUC1) and the method to make it.

For a vector, one description is its sequence, however, there is no disclosure about the sequence of rV-MUC1. Next, then, it is determined whether the invention has been sufficiently described by other relevant identifying characteristics (i.e. other than nucleotide sequence). In the instant case, the description disclosed in the specification is not sufficient to describe the characteristics of the vector, for example, its map or restriction sites or sequence elements of the virus.

This limited information is not deemed sufficient to reasonably convey to one skilled in the art that Applicant is in possession of cDNAs besides Seq ID No 1 and 3 that encode the amino acid sequences disclosed in Seq ID No 2 and 4 respectively, at the time the application was filed. Thus it is concluded that the written description requirement is not satisfied for the claimed genus.

6. Claim 38 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 38 limits the virus of claim 23 to rV-MUC1.

As noted in previous paragraphs, to determine whether a specification meets the enablement requirements, some of the factors to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is "undue".

In the instant case the invention is a recombinant pox virus, named rV-MUC1.

The specification is not enabling for the claimed invention because based on the information provided in the specification, an artisan of skill would not have been

able to construct the claimed recombinant pox virus without undue experimentation.

The specification on page 22 discloses 22 that miniMUC1 gene was inserted 3' to the vaccinia 40K early/late promoter and flanked by sequences from Hind III M region of the vaccinia genome. The resulting plasmid, pT2041,contained the miMUC1 gene under the control of the vaccinia virus 40k early/late promoter flanked by DNA sequences from the Hind III M region of the vaccinia genome. The question is: would an artisan of skill have been able to make the said plasmid, with the disclosed information without undue experimentation because to clone a fragment of DNA in another DNA one requires the information regarding the restriction site of both the DNAs or some references where both the DNA fragments have been described. In the instant case, while the specification discloses the MUC1 fragment, the description of the vaccinia virus is not sufficient, for example, at what position 3' to the promoter was the MUC1 inserted, were both the promoters functional or only one was or whether the promoters were functional et al. Likewise, what sequences from the Hind III M region of the vaccinia virus were present in the recombinant vector. While an artisan may be able to make some recombinant vaccinia virus comprising MUC1 fragment, with the disclosure as filed, an artisan may not be able to make the rV-MUC1 vector in the absence of the specific information, such as, restriction map, strain of the vaccinia virus etc.

The application discloses vector rV-MUC1 that is encompassed by the definitions for **biological material** set forth in 37 C.F.R. § 1.801. Because it is apparent that this biological material is essential for practicing the claimed invention, it must be obtainable by a reproducible method set forth in the specification or otherwise be known and readily available to the public as detailed in 37 C.F.R. §§ 1.801 through 1.809.

It is unclear whether this biological material is known and readily available to the public or that the written instructions are sufficient to reproducibly construct this biological material from starting materials known and readily

available to the public. Accordingly, availability of such biological material is deemed necessary to satisfy the enablement provisions of 35 U.S.C. § 112. If this biological material is not obtainable or available, the requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the biological material. In order for a deposit to meet all criteria set forth in 37 C.F.R. §§ 1.801-1.809, applicants or assignee must provide assurance of compliance with provisions of 37 C.F.R. §§ 1.801-1.809, in the form of a declaration or applicant's representative must provide a statement. The content of such a declaration or statement is suggested by the enclosed attachment. Because such deposit will not have been made prior to the effective filing date of the instant application, applicant is required to submit a verified statement from a person in a position to corroborate the fact, which states that the biological material which has been deposited is the biological material specifically identified in the application as filed (37 C.F.R. § 1.804). Such a statement need not be verified if the person is an agent or attorney registered to practice before the Office. Applicant is also reminded that the specification must contain reference to the deposit, including deposit (accession) number, date of deposit, name and address of the depository, and the complete taxonomic description.

In conclusion, the specification fails to disclose sufficient guidance so an artisan of skill would have been able to make the claimed recombinant vaccinia virus rV-MUC1 without undue experimentation and use it as claimed.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 23-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 23 and 27 and their respective dependent claims are indefinite because they recite the term "approximately". The metes and bounds of the claimed invention can not be assessed because the term "approximately" is a relative term and approximately 7-15 or 5-25 could be interpreted as 1-25 or 1-15 etc.

Claims 23 and 27 are vague and indefinite because the metes and bounds of the term "wherein said nucleic acid is altered from the native tandem repeat pattern" is not clear.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 23-25 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Acres et al (Acres RB et al. Journal of Immunotherapy 14:136-143, 1993).

Acres et al immunization of mice with a vaccinia virus that expression a MUC1 fragment that has 4 tandem repeat units. Mice immunized with this construct produce antibodies that recognize MUC1 and 30% mice which were immunized with MUC1 are protected from growth of p815-MUC1 tumors when implanted with tumor cells (see the summary). Acres also teaches administration of the virus i.p. (see materials and methods).

The claimed invention recites approximately 5-25 repeats, which is interpreted as 4 repeats. Therefore, the invention of claims 23-25 and 27 are anticipated by Acres et al.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 23-37 and 39-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Acres et al as applied to claim 1-3 above, and further in view of Paoletti E (US 5,942,235, dated 8-24-00, effective filing date 6-2-1995) and Bronte et al (Journal of Immunology 154:5282-5292, 1995) and Gunaburg et al (Molecular Medicine Today 1:410-417, 1995).

Acres et al immunization of mice with a vaccinia virus that expression a MUC1 fragment that has 4 tandem repeat units. Mice immunized with this construct produce antibodies that recognize MUC1 and 30% mice which were immunized with MUC1 are protected from growth of p815-MUC1 tumors when implanted with tumor cells (see the summary). Acres also administration the virus i.p. (see materials and methods). Acres et al do not teach an orthopox, suipox or avipox virus for expressing MUC1 fragment.

At the time of the claimed invention, Paoletti et al taught recombinant poxvirus vectors for inducing immune responses (see summary and the claims). This prior art further teaches that the virus can include within a non-essential region of the virus genome, a heterologous DNA sequence which encodes an antigenic protein, e.g. derived from a pathogen, a tumor associated antigen, a cytokine or combination thereof. The virus used in the vaccine according to the present invention is advantageously a poxvirus, particularly a vaccinia virus or an avipox virus, such as a fowlpox virus and a canarypox virus. The attenuated virulence of the vector advantageously reduces the opportunity for the possibility of a runaway infection due to vaccination in the vaccinated individual. Paoletti et al

also teach the recombinant pox virus vectors expressing human melanoma-associated antigen MZ2-E (example 16), IL-2 alone (example 18) or IL-2 plus INF-gamma (example 22), B7 (example 28).

Additionally, Bronte V et al taught a recombinant poxvirus vector which comprises the cDNA encoding both IL-2 and tumor associated antigen (TAA). This prior art also compared the effects of immunization of a mouse with a pox virus expressing TAA and providing the animal with IL-2 (expressed from another vector) separately with mice wherein both IL-2 and TAA were supplied by the same pox virus vector and with mice which received TAA pox virus vector alone. Their results showed that the therapeutic effects of the combination of poxvirus and IL-2 was greater than either of these treatments alone. When the cDNA for IL-2 was inserted in the genome of the vaccinia virus to a make a double recombinant, antitumor activity was further augmented (see the abstract and rest of the article).

Gunzburg et al review the state of the art of virus vector design in gene therapy (see the entire article).

Accordingly it would have been obvious to one of ordinary skill in the art to modify the vector of Acres et al according to Paolotti et al and Bronte et al wherein both MUC1 and IL-2 would have bee expressed on one vector or by separate vectors and immunize a mouse with such a vector because vectors based on Paolotti et al would have less virulence whereas modification of the vectors according to Bronte et al would have produced a better immunization of the mouse, due to the expression of immunemodulator IL-2 or B4, when administered and provided with a booster dose. Additionally, it would have been obvious to one of ordinary skill in the art trying to immunize an animal with MUC1 to provide the first immunizing dose of MUC1 via one pox viral vector, followed by another pox viral vector that could be same or a different pox virus vector, as reviewed by Gunzburg et al because at the time of the invention, viral vectors were routinely used in experimental animals for producing viral protein in vivo and then to provide the booster dose with another pox virus. An artisan would be motivated to use one

vector in the first step of immunization to produce large amounts of the MUC1 protein whereas the second pox virus based expression vector would produce MUC1 sufficient for the booster dose.

Therefore, the claimed invention as a whole would have been *prima facie* to one of ordinary skill in the art at the time the invention was made in the absence of evidence to the contrary.

13. No claim is allowed.

14. The article by Scholl et al (Journal of Immunotherapy 23:570-580, 2000) is of interest as it teaches immunotherapy in patients with a recombinant vaccinia virus that encodes human MUC1 and IL-2.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (571) 272-0735 . The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. The fax phone number for TC 1600 is (703) 872-9306. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the Dianiece Jacobs whose telephone number is (571) 272-0532.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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